```
=> d his

     (FILE 'HOME' ENTERED AT 11:28:06 ON 28 FEB 2008)

     FILE 'REGISTRY' ENTERED AT 11:28:14 ON 28 FEB 2008
L1              STRUCTURE UPLOADED
L2            0 S L1
L3              STRUCTURE UPLOADED
L4            0 S L3
L5              STRUCTURE UPLOADED
L6            0 S L5
L7           10 S L5 SSS FUL
L8           10 S L7 AND CAPLUS/LC

     FILE 'CAPLUS' ENTERED AT 11:31:54 ON 28 FEB 2008
L9            1 S L7

=> d ibib abs hitstr total
```

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:550951 CAPLUS
DOCUMENT NUMBER: 141:89120
TITLE: Preparation of substituted 4-(4-piperidin-4-yl-piperazin-1-yl)-azepane derivatives and their use as neurokinin antagonists
INVENTOR(S): Janssens, Frans Eduard; Sommen, Francois Maria; De Boeck, Benoit Christian Albert Ghislain; Leenaerts, Joseph Elisabeth
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056805	A1	20040708	WO 2003-EP51043	20031217
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2509090	A1	20040708	CA 2003-2509090	20031217
AU 2003298369	A1	20040714	AU 2003-298369	20031217
EP 1578744	A1	20050928	EP 2003-796109	20031217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006512350	T	20060413	JP 2004-561506	20031217
US 2006058285	A1	20060316	US 2005-540456	20050622
PRIORITY APPLN. INFO.:			WO 2002-EP14834 A	20021223
			WO 2003-EP51043 W	20031217

OTHER SOURCE(S): MARPAT 141:89120
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

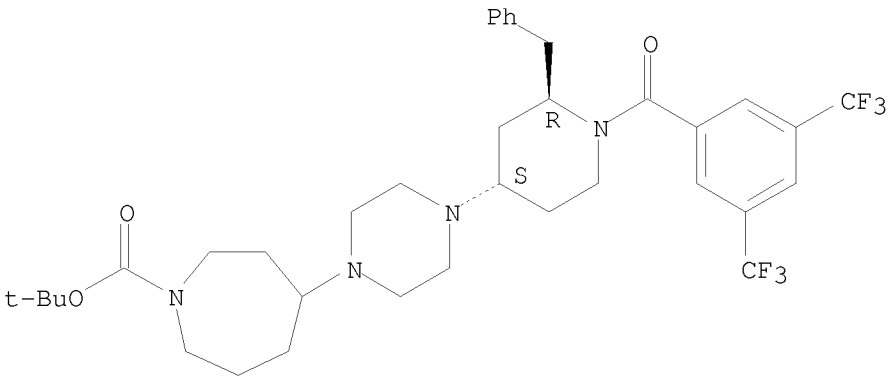
AB Title compds. I [Q = O or NR3; X = covalent bond, -O-, -S-, or -NR3; R1 independently = Ar1, Ar1-alkyl, and di(Ar1)-alkyl; R2 = Ar2, Ar2-alkyl, di(Ar2)-alkyl Het1, Het1-alkyl; R3 independently = H or alkyl; Y = covalent bond, -CO-, -SO2-, >C:CHR or >C:NR, wherein R = H, CN or NO2; M independently = covalent bond, (un)substituted-alkyl, -(un)saturated carbocycle; L = H, alkyloxy, Ar3oxy, alkylamine, etc.; Ar1 = (un)substituted phenyl; Ar2 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, aminocarbonyl, and alkyloxy; Ar3 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, amino, alkyloxy, OH, pyridinyl, etc.; Het1 = monocyclic

heterocyclic radical selected from pyrrolyl, pyrazolyl, imidazolyl, furanyl, etc.; m = 1 or 2 provided that if m = 2, then n = 1; n = 0-2; p = 1-2; q = 0-1] and their pharmaceutically acceptable salts having neurokinin antagonistic activity, in particular NK1 antagonistic activity, their preparation, compns. comprising them and their use as a medicine, in particular for the treatment of pain, emesis, anxiety, depression and IBS are disclosed. Thus, e.g., II was prepared via resolution of intermediate III (preparation given), de-N-benzylation, and reaction with 4-oxoazepan-1-carboxylic acid tert-Bu ester. The receptor binding values (pIC50) for the h-NK1 ranges for all compds. according to the invention between 10 and 6. In view of their capability to antagonize the actions of tachykinins by blocking the neurokinin receptors, and in particular antagonizing the actions of substance P and Neurokinin B by blocking the NK1, NK2 and NK3 receptors, the compds. according to the invention are useful as a medicine, in particular in the prophylactic and therapeutic treatment of tachykinin-mediated conditions, such as, for instance CNS disorders, in particular schizoaffective disorders, depression, anxiety disorders, stress-related disorders, sleep disorders, cognitive disorders, personality disorders, eating disorders, neurodegenerative diseases, addiction disorders, mood disorders, sexual dysfunction, pain and other CNS-related conditions ; inflammation ; allergic disorders ; emesis ; gastrointestinal disorders, in particular irritable bowel syndrome (IBS); skin disorders ; vasospastic diseases ; fibrosing and collagen diseases ; disorders related to immune enhancement or suppression and rheumatic diseases and body weight control.

IT 717129-41-4P 717129-45-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; stereoselective preparation of piperidinylpiperazinylazepanes with tachykinin antagonist activity)

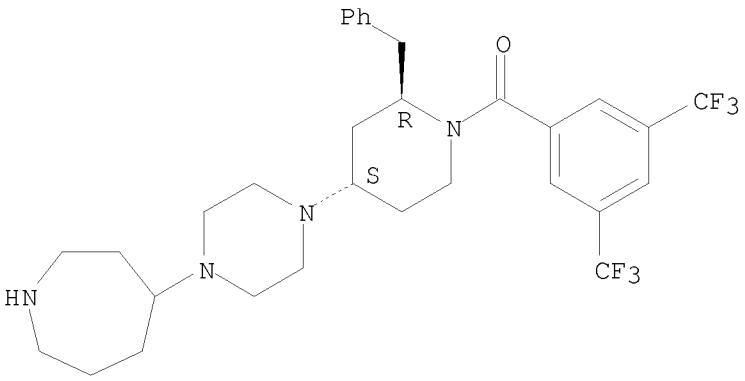
RN 717129-41-4 CAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]hexahydro-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



RN 717129-45-8 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-(hexahydro-1H-azepin-4-yl)-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

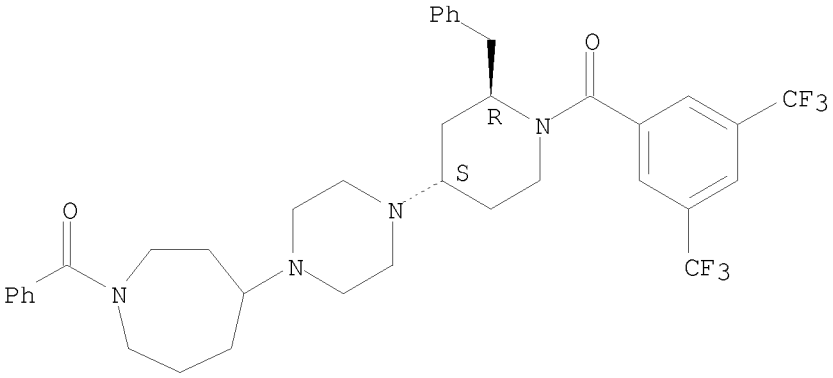


IT 717129-49-2P 717129-54-9P 717129-58-3P
717129-64-1P 717129-68-5P 717129-70-9P
717129-74-3P 717129-77-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; stereoselective preparation of piperidinylpiperazinylazepanes with tachykinin antagonist activity)

RN 717129-49-2 CAPLUS

CN 1H-Azepine, 1-benzoyl-4-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]hexahydro- (9CI) (CA INDEX NAME)

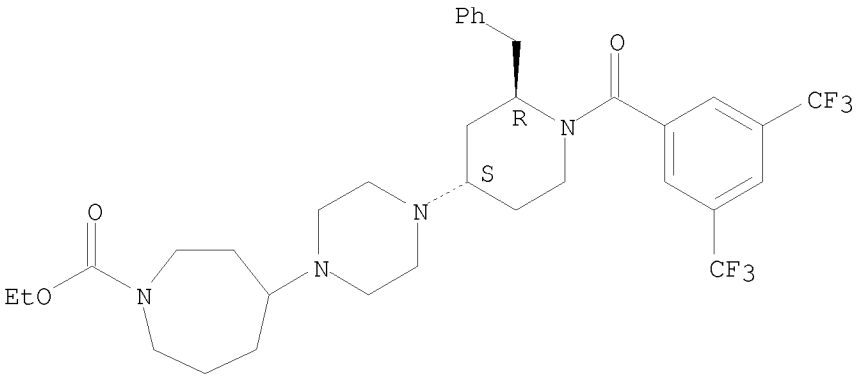
Absolute stereochemistry.



RN 717129-54-9 CAPLUS

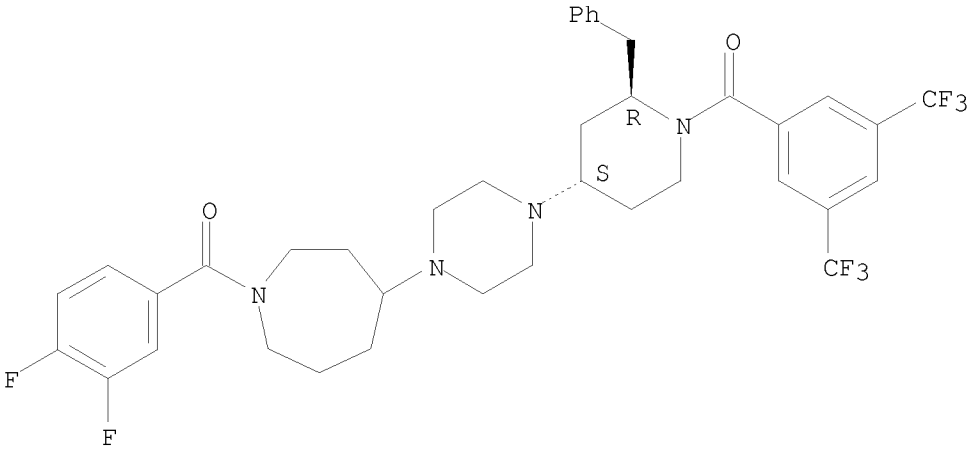
CN 1H-Azepine-1-carboxylic acid, 4-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]hexahydro-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



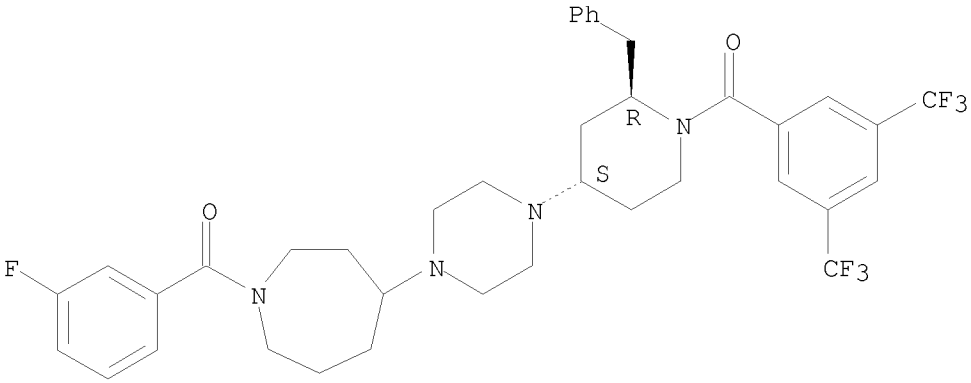
RN 717129-58-3 CAPLUS
CN 1H-Azepine, 4-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]-1-(3,4-difluorobenzoyl)hexahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



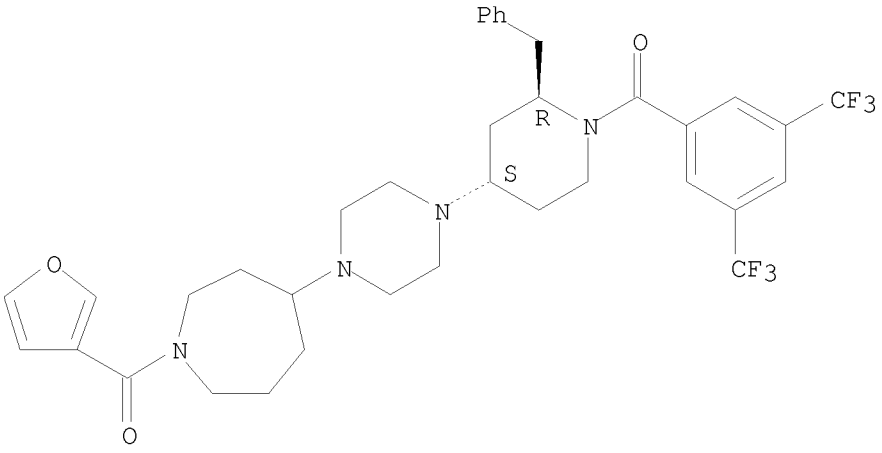
RN 717129-64-1 CAPLUS
CN 1H-Azepine, 4-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]-1-(3-fluorobenzoyl)hexahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



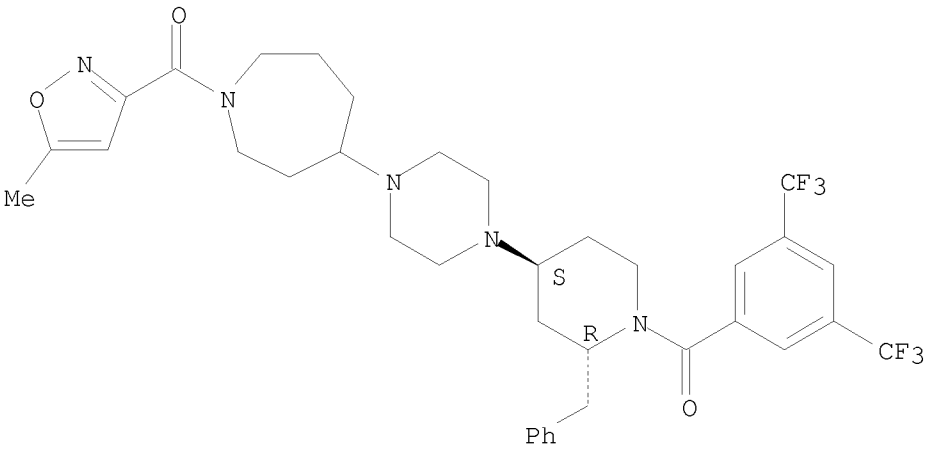
RN 717129-68-5 CAPLUS
CN 1H-Azepine, 4-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]-1-(3-furanylcarbonyl)hexahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



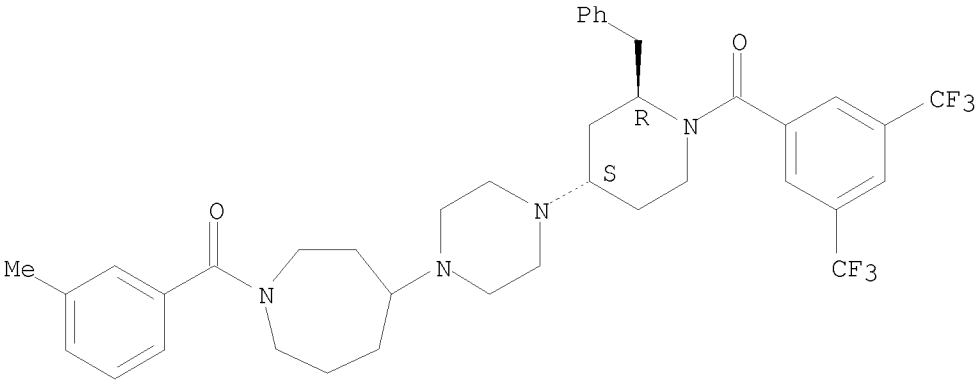
RN 717129-70-9 CAPLUS
CN 1H-Azepine, 4-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]hexahydro-1-[(5-methyl-3-isoxazolyl)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



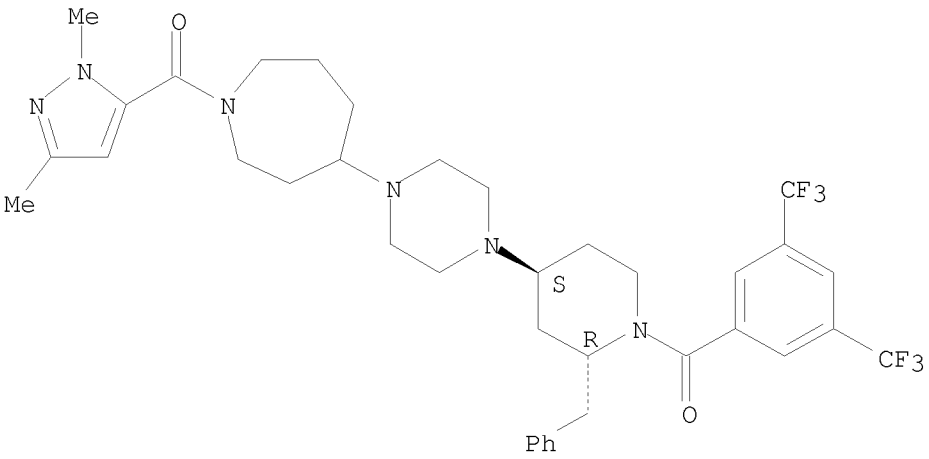
RN 717129-74-3 CAPLUS
CN 1H-Azepine, 4-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]hexahydro-1-(3-methylbenzoyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 717129-77-6 CAPLUS
CN 1H-Azepine, 4-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]-1-[(1,3-dimethyl-1H-pyrazol-5-yl)carbonyl]hexahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT